

**SYNLETT**

**Spotlight 311**

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research.

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**N,N’-Dimethyl Urea**

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**Introduction**

*N,N’*-Dimethyl urea (DMU) (1,3-dimethyl urea, methyl carbamide) is a colourless solid and a non-volatile, versatile and powerful reagent for the synthesis of nitrogen-containing heterocyclic compounds. It is used for the synthesis of caffeine, theophylline, pharmaceuticals, textile aids, herbicides, etc. It also finds application in metal-ion complexation, material science, etc. In 1954, Blick and Godt synthesized the important building block *N,N’*-dimethyl-6-amino uracil from a mixture of DMU, cyanoacetic acid, and acetic anhydride with exclusion of moisture under stirring at 60 °C for 3 h. It is a very important starting material for the synthesis of pyrimidine derivatives.

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**Preparation**

DMU can be prepared by the reaction of methylamine with carbon dioxide (Scheme 1). In 1939, Grinberg reported the first synthesis of alkyl-substituted carbamides by reaction between NO2CONHNO2 and methylamine. Shigeru and co-workers introduced an easy and reliable method in 1978 by treating methylamine with carbon dioxide at -30 to -50 °C for 24 h, followed by heating at an average rate of 3 °C/min in an autoclave.

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**Abstracts**

(A) The synthesis of 4-aryl-3,4-dihydropyrimidines (Biginelli compounds, DHPMS) is accomplished by heating a solvent-free mixture of an aldehyde, an active methylene compound, DMU, and Dowex-50W ion-exchange resin.

(B) The simple heating of two equivalents of phenyl acetaldehyde with DMU in the presence of BF3·OEt2 (10 mol%) as a catalyst in toluene afforded dihydropyrimidinone in 92% yield.

(C) The reaction between o-bromo benzoate and DMU in the presence of Xantphos as the initial ligand and the weak base Cs2CO3 provided the quinazolinedione in 90% yield.

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**Scheme 1**

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\text{MeNH}_2 + \text{CO}_2 \rightarrow \text{MeNHCO}_2\text{NH}_3\text{Me} \]

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(D) The interaction of 1,3-dimethylbarbituric acid, glyoxals, and DMU in methanol with a catalytic amount of glacial acetic acid led to 5-(5-aryl-1,3-dimethyl-2-oxo-2,3-dihydro-1H-imidazol-4-yl)-1,3-dimethylpyrimidine-2,4,6-triones.\(^7\)

(E) \(N\)-methyl imines can be synthesized by the reaction of DMU and aldehydes in the presence of solid clay-montmorillonite K10.\(^8\)

(F) The regioisomeric diene DMU 1,2-adducts \(A/B\) were synthesized by reacting isoprene with DMU using palladium(II) catalyst \((\text{O}_2/\text{cat.})\) (method A). Switching from oxygen to benzoquinone as reoxidant avoids the generation of water and affords 1,2-adducts \(A/B\) in good yield (method B).\(^9\)

(G) The conversion of benzylamine into the triazone derivative was achieved by reflux condensation with DMU and aqueous formaldehyde under argon atmosphere and heating at 100 °C for 16 h.\(^{10}\)

(H) The addition of DMU to a mixture of isocyanide and acid chloride gave formamidine urea salts in pure form.\(^{11}\)

(I) The coupling reaction between 2-chloropyridine and DMU gives primarily the corresponding mono-coupled urea.\(^{12}\)

(J) Kolos and co-workers synthesized 4-aryl-5-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-imidazol-2(3H)-ones by one-pot condensation of 4-hydroxycoumarin with arylglyoxals and DMU in ethanol in the presence of a catalytic amount of acetic acid within a short time (15–50 min).\(^{13}\)

References